At page 6, line 19, please delete the entire section entitled "Brief Description of the Figures."

At page 7, line 15, please replace the entire paragraph beginning "[t]he present invention provides" with the following amended paragraph:

C2

--The present invention provides isolated nucleic acid molecules comprising a polynucleotide encoding TR18, such as, for example, polynucleotides having the nucleotide sequence shown in SEQ ID NO:1. The present invention provides isolated nucleic acid molecules comprising a polynucleotide encoding a TR18 polypeptide having the amino acid sequence shown in SEQ ID NO:2.--

At page 7, line 22, please replace the entire paragraph beginning "[t]he determined nucleotide sequence" with the following amended paragraph:

C3

--The determined nucleotide sequence of TR18 (SEQ ID NO:1) contains an open reading frame encoding a protein of about 184 amino acid residues, with a deduced molecular weight of about 20.1 kDa. The amino acid sequence of the predicted mature TR18 receptor is shown in SEQ ID NO:2 from amino acid residue about 1 to residue about 184.--

At page 8, line 5, please replace the entire paragraph beginning "[t]he present invention provides" with the following amended paragraph:

C4

--The present invention provides a nucleotide sequence encoding the mature TR18 polypeptide having the amino acid sequence shown in SEQ ID NO:2. By the mature TR18 protein having the amino acid sequence shown in SEQ ID NO:2 is meant the mature form(s) of the TR18 receptor predicted by computer analysis or produced by expression of the coding sequence shown in SEQ ID NO:2 in a mammalian cell (e.g., COS cells, as described below). As indicated below, the mature TR18 receptor having the amino acid sequence encoded by the coding sequence shown in SEQ ID NO:2 may or may not differ from the predicted mature TR18 protein shown in SEQ ID NO:2 (amino acids from about 1 to about 184) depending on the accuracy of the predicted cleavage site based on computer analysis.--

At page 8, line 21, please replace the entire paragraph beginning "[t]he polypeptide sequence" with the following amended paragraph:

-- The polypeptide sequence of the TR18 depicted in SEQ ID NO:2 can routinely be examined by computer programs. For example, the mature form, intracellular form, extracellular form, and transmembrane domains of the TR18 polypeptides of the invention can routinely be predicted via analysis using the "PSORT" computer program (K. Nakai and M. Kanehisa, *Genomics* 14:897-911 (1992)), which is an expert system for predicting the cellular location of a protein based on the amino acid sequence. As part of this computational prediction of localization, the methods of McGeoch and von Heinje are incorporated into the PSORT program.--

C5

At page 8, line 29, please replace the entire paragraph beginning "[t]he predicted TR18 polypeptide," and extending onto page 9, with the following amended paragraph:

--The predicted TR18 polypeptide comprises about 184 amino acids. However, as one of ordinary skill in the art would appreciate, the actual TR18 polypeptide may be anywhere in the range of 174-194 amino acids due to the possibilities of sequencing errors as well as the variability of cleavage sites for leaders in different known proteins. It will further be appreciated that, the domains described herein have been predicted by computer analysis, and accordingly, that depending on the analytical criteria used for identifying various functional domains, the exact "address" of, for example, the extracellular domain, intracellular domain, cysteine-rich motif, and transmembrane domain of TR18 may differ slightly from the predicted locations. For example, the exact location of the TR18 extracellular domain in SEQ ID NO:2 may vary slightly (e.g., the address may "shift" by about 1 to about 20 residues, more likely about 1 to about 5 residues) depending on the criteria used to define the domain. In any event, as discussed in more detail below, the invention further provides polypeptides having various residues deleted from the N-terminus and/or C-terminus of the complete TR18 polypeptide, including polypeptides lacking one or more amino acids from the N-termini of the TR18 extracellular domains described herein, which constitute soluble forms of the extracellular domain of the TR18 polypeptides respectively.--

C6

At page 10, line 3, please replace the entire paragraph beginning "[i]solated nucleic acid molecules," with the following amended paragraph:

C7

--Isolated nucleic acid molecules of the present invention include DNA molecules comprising an open reading frame (ORF) shown in SEQ ID NO:1; DNA molecules comprising the coding sequence for the complete (full-length) and/or mature TR18 protein shown in SEQ ID NO:2; and DNA molecules which comprise a sequence substantially different from those described above, but which, due to the degeneracy of the genetic code, still encode the TR18 protein. Of course, the genetic code is well known in the art. Thus, it would be routine for one skilled in the art to generate such degenerate variants.--

At page 10, line 11, please replace the entire paragraph beginning "[t]he invention further provides," with the following amended paragraph:

C8

--The invention further provides an isolated nucleic acid molecule having the nucleotide sequence shown in SEQ ID NO:1, or a nucleic acid molecule having a sequence complementary thereto. Such isolated molecules, particularly DNA molecules, are useful, for example, as probes for gene mapping by *in situ* hybridization with chromosomes, and for detecting expression of the TR18 gene in human tissue, for instance, by Northern blot analysis.--

At page 10, line 17, please replace the entire paragraph beginning "[t]he present invention is further," and extending onto page 11, with the following amended paragraph:

C9

--The present invention is further directed to fragments of the isolated nucleic acid molecules described herein. By a fragment of an isolated DNA molecule having the nucleotide sequence of the nucleotide sequence shown in SEQ ID NO:1 is intended DNA fragments at least about 15 nt, and more preferably at least about 20 nt, at least about 24 nt, still more preferably at least about 30 nt, at least about 35 nt, and even more preferably, at least about 40 nt, at least about 45 nt, at least about 50 nt, at least about 55 nt, at least about 60 nt, at least about 65 nt, at least about 70 nt, at least about 75 nt, at least about 100 nt, at least about 150 nt, at least about 200 nt, at least about 250 nt, at least about 300 nt in length which are useful, for example, as diagnostic probes and primers as discussed herein. Of course, larger fragments 350-833 nt in length are also useful according to the present invention, as are fragments corresponding to most, if not all, of the nucleotide

sequence as shown in SEQ ID NO:1, or the complementary strand thereto. By a fragment at least 20 nt in length, for example, is intended fragments which include 20 or more contiguous bases from the nucleotide sequence of the nucleotide sequence as shown in SEQ ID NO:1. In this context "about" includes the particularly recited size, and sizes larger or smaller by several (5, 4, 3, 2, or 1) nucleotides, at either terminus or at both termini. In specific embodiments, the fragments of the invention comprise, or alternatively consist of, nucleotides 91-105, 148 to 159, 211 to 222, 379 to 399, 463 to 492, 543 to 564 of SEQ ID NO:1 or the complementary strand thereto. Polypeptides encoded by these polynucleotide are also encompassed.--

C9

At page 11, line 6, please replace the entire paragraph beginning "[r]epresentative examples," with the following amended paragraph:

--Representative examples of TR18 polynucleotide fragments of the invention include, for example, fragments that comprise, or alternatively, consist of, a sequence from about nucleotide 1 to 33, 34 to 66, 67 to 87, 88 to 120, 121 to 156, 157 to 189, 190 to 228, 229 to 255, 256 to 282, 283 to 306, 307 to 336, 337 to 369, 370 to 399, 400 to 432, 433 to 462, 463 to 495, 496 to 525, 526 to 558, 559 to 588, 589 to 618, 619 to 648, 649 to 678, 679 to 711, 712 to 741, 742 to 771, 772 to 804, and/or 805 to 834 of SEQ ID NO:1, or the complementary strand thereto. In this context "about" includes the particularly recited ranges, and ranges larger or smaller by several (5, 4, 3, 2, or 1) nucleotides, at either terminus or at both termini.--

C10

At page 11, line 15, please replace the entire paragraph beginning "[i]n specific embodiments," with the following amended paragraph:

--In specific embodiments, the polynucleotide fragments of the invention comprise, or alternatively, consist of, a sequence from nucleotide 88 to 189, of SEQ ID NO:1, or the complementary strand thereto.--

C11

At page 12, line 31, please replace the entire paragraph beginning "[p]referred nucleic acid fragments," and extending onto page 13, with the following amended paragraph:

C12

--Preferred nucleic acid fragments of the present invention include nucleic acid molecules encoding a member selected from the group: a polypeptide comprising or alternatively, consisting of, the TR18 receptor extracellular domain (amino acid residues from about 1 to about 54 in SEQ ID NO:2; a polypeptide comprising, or alternatively consisting of, the TR18 cysteine rich domain (amino acid residues from about 8 to about 41 in SEQ ID NO:2); a polypeptide comprising, or alternatively consisting of the TR18 transmembrane domain (amino acid residues from about 55 to about 80 in SEQ ID NO:2; and/or a polypeptide comprising, or alternatively consisting of, the TR18 intracellular domain (amino acid residues from about 81 to about 184 in SEQ ID NO:2). Since the locations of these domains have been predicted by computer analysis, one of ordinary skill would appreciate that the amino acid residues constituting these domains may vary slightly (e.g., by about 1 to 15 amino acid residues) depending on the criteria used to define each domain.--

At page 13, line 13, please replace the entire paragraph beginning "[p]referred nucleic acid fragments of the invention," with the following amended paragraph:

C13

--Preferred nucleic acid fragments of the invention encode a full-length TR18 polypeptide lacking the nucleotides encoding the amino terminal methionine in SEQ ID NO:1, as it is known that the methionine is cleaved naturally and such sequences may be useful in genetically engineering TR18 expression vectors. Polypeptides encoded by such polynucleotides are also contemplated by the invention.--

At page 13, line 18, please replace the entire paragraph beginning "[p]referred nucleic acid fragments of the present invention," and extending onto page 14, with the following amended paragraph:

C14

--Preferred nucleic acid fragments of the present invention further include nucleic acid molecules encoding epitope-bearing portions of the TR18 receptor proteins. In particular, such nucleic acid fragments of the present invention include nucleic acid molecules encoding: a polypeptide comprising amino acid residues from

about 9 to about 13 in SEQ ID NO:2; a polypeptide comprising amino acid residues from about 28 to about 31 in SEQ ID NO:2; a polypeptide comprising amino acid residues from about 49 to about 52 in SEQ ID NO:2; a polypeptide comprising amino acid residues from about 105 to about 111 in SEQ ID NO:2; a polypeptide comprising amino acid residues from about 133 to about 142 in SEQ ID NO:2; and a polypeptide comprising amino acid residues from about 160 to about 166 in SEQ ID NO:2. In this context "about" includes the particularly recited ranges, and ranges larger or smaller by several (5, 4, 3, 2, or 1) nucleotides, at either terminus or at both termini. The inventors have determined that the above polypeptide fragments are antigenic regions of the TR18 proteins. Methods for determining other such epitope-bearing portions of the TR18 proteins are described in detail below.--

C14

At page 14, line 2, please replace the entire paragraph beginning "[i]t is believed," with the following amended paragraph:

--It is believed that the extracellular cysteine rich motifs of TR18 disclosed in SEQ ID NO:2 are important for interactions between TR18 and its ligands (e.g., Neutrokine alpha and APRIL). Accordingly, specific embodiments of the invention are directed to polynucleotides encoding polypeptides which comprise, or alternatively consist of, the amino acid sequence of amino acid residues 8 to 41 of SEQ ID NO:2. Polypeptides encoded by these polynucleotides are also encompassed by the invention.--

C15

At page 14, line 15, please replace the entire paragraph beginning "[t]he data representing," with the following amended paragraph:

--The data representing the structural or functional attributes of TR18 set forth in Table I, as described above, was generated using the various modules and algorithms of the DNA*STAR set on default parameters. In a preferred embodiment, the data presented in columns VIII, XI, XIII and XIV of Table I can be used to determine regions of TR18 which exhibit a high degree of potential for antigenicity. Regions of high antigenicity are determined from the data presented in columns VIII, XI, XIII and/or XIV by choosing values which represent regions of the polypeptide which are likely to be exposed on the surface of the polypeptide

C16

C16

in an environment in which antigen recognition may occur in the process of initiation of an immune response.--

At page 14, line 24, please replace the entire paragraph beginning "[c]ertain preferred regions," with the following amended paragraph:

C17

--Certain preferred regions in these regards may be represented or identified by using tabular representations of the data presented in Table I. The DNA*STAR computer algorithm used to generate Table I (set on the original default parameters) was used to present the data in a tabular format (See Table I). The tabular format of the data may be used to easily determine specific boundaries of a preferred region.--

At page 14, line 30, please replace the entire paragraph beginning "[t]he above-mentioned preferred regions," and extending onto page 15, with the following amended paragraph:

C18

--The above-mentioned preferred regions set out in Table I, include, but are not limited to, regions of the aforementioned types identified by analysis of the amino acid sequences set out in SEQ ID NO:2. As set out in Table I, such preferred regions include Garnier-Robson alpha-regions, beta-regions, turn-regions, and coil-regions, Chou-Fasman alpha-regions, beta-regions, and turn-regions, Kyte-Doolittle hydrophilic regions, Hopp-Woods hydrophobic regions, Eisenberg alpha- and beta-amphipathic regions, Karplus-Schulz flexible regions, Jameson-Wolf regions of high antigenic index and Emini surface-forming regions. --

At page 18, line 25, please replace the entire paragraph beginning "[b]y a polynucleotide which hybridizes," with the following amended paragraph:

C19

--By a polynucleotide which hybridizes to a "portion" of a polynucleotide is intended a polynucleotide (either DNA or RNA) hybridizing to at least about 15 nucleotides (nt), and more preferably at least about 20 nt, still more preferably at least about 30 nt, and even more preferably about 30-70 nt of the reference polynucleotide. These are useful, for example, as diagnostic probes and primers as discussed above and in more detail below. By a portion of a polynucleotide of "at least 20 nt in length," for example, is intended 20 or more contiguous nucleotides from the nucleotide sequence of the reference polynucleotide (e.g., the nucleotide

sequence as shown in SEQ ID NO:1. In this context "about" includes the particularly recited size, and sizes larger or smaller by several (5, 4, 3, 2, or 1) nucleotides, at either terminus or at both termini.--

C19

At page 19, line 1, please replace the entire paragraph beginning "[i]n further embodiments," with the following amended paragraph:

--In further embodiments, polynucleotides of the invention comprise at least 15, at least 30, at least 50, at least 100, or at least 250, at least 500, or at least 800 contiguous nucleotides of TR18 coding sequence, but consist of less than or equal to 100 kb, 75 kb, 50 kb, 30 kb, 25 kb, 20 kb, 15 kb, 10 kb, or 5 kb of genomic DNA that flanks the 5' or 3' coding nucleotide set forth in SEQ ID NO:1. In further embodiments, polynucleotides of the invention comprise at least 15, at least 30, at least 50, at least 100, or at least 250, at least 500, or at least 800 contiguous nucleotides of TR18 and/or coding sequence, but do not comprise all or a portion of any TR18 intron. In another embodiment, the nucleic acid comprising TR18 coding sequence does not contain coding sequences of a genomic flanking gene (i.e., 5' or 3' to the TR18 gene in the genome). In other embodiments, the polynucleotides of the invention do not contain the coding sequence of more than 1000, 500, 250, 100, 50, 25, 20, 15, 10, 5, 4, 3, 2, or 1 genomic flanking gene(s).--

C20

At page 20, line 15, please replace the entire paragraph beginning "[f]urther embodiments of the invention," with the following amended paragraph:

--Further embodiments of the invention include isolated nucleic acid molecules comprising, or alternatively consisting of, a polynucleotide having a nucleotide sequence at least 80%, 85%, or 90% identical, and more preferably at least 95%, 96%, 97%, 98%, or 99% identical to: (a) a nucleotide sequence encoding the polypeptide having the amino acid sequence shown in SEQ ID NO:2; (b) a nucleotide sequence encoding the polypeptide having the amino acid sequence in SEQ ID NO: 2, but lacking the amino terminal methionine; (c) a nucleotide sequence encoding the polypeptide having the amino acid sequence at positions 1 to 184 in SEQ ID NO:2; (d) a nucleotide sequence encoding the TR18 extracellular domain; (e) a nucleotide sequence encoding the TR18 rich motif (i.e., amino acid residues 8 to 41 in SEQ ID NO:2); (f) a nucleotide sequence encoding the TR18 transmembrane domain; (g) a nucleotide sequence encoding the TR18 receptor

C21

intracellular domain; (h) a nucleotide sequence encoding the TR18 receptor extracellular and intracellular domains with all or part of the transmembrane domain deleted; and (i) a nucleotide sequence complementary to any of the nucleotide sequences in (a), (b), (c), (d), (e), (f), (g), or (h) above. Polypeptides encoded by these polynucleotides are also encompassed by the invention.--

C21

At page 20, line 31, please replace the entire paragraph beginning "[b]y a polynucleotide having," and extending onto page 21, with the following amended paragraph:

--By a polynucleotide having a nucleotide sequence at least, for example, 95% "identical" to a reference nucleotide sequence encoding a TR18 polypeptide is intended that the nucleotide sequence of the polynucleotide is identical to the reference sequence except that the polynucleotide sequence may include up to five mismatches per each 100 nucleotides of the reference nucleotide sequence encoding the TR18 polypeptide. In other words, to obtain a polynucleotide having a nucleotide sequence at least 95% identical to a reference nucleotide sequence, up to 5% of the nucleotides in the reference sequence may be deleted or substituted with another nucleotide, or a number of nucleotides up to 5% of the total nucleotides in the reference sequence may be inserted into the reference sequence. These mismatches of the reference sequence may occur at the 5' or 3' terminal positions of the reference nucleotide sequence or anywhere between those terminal positions, interspersed either individually among nucleotides in the reference sequence or in one or more contiguous groups within the reference sequence. The reference (query) sequence may be the entire TR18 encoding nucleotide sequence shown in SEQ ID NO:1, or any TR18 polynucleotide fragment (e.g., a polynucleotide encoding the amino acid sequence of any of the TR18 N- and/or C-terminal deletions described herein), variant, derivative or analog, as described herein.--

C22

At page 21, line 17, please replace the entire paragraph beginning "[a]s a practical matter," with the following amended paragraph:

--As a practical matter, whether any particular nucleic acid molecule is at least 80%, 85%, 90%, 92%, 95%, 96%, 97%, 98% or 99% identical to, for instance, the nucleotide sequence shown in SEQ ID NO:1 can be determined conventionally

C23

using known computer programs such as the Bestfit program (Wisconsin Sequence Analysis Package, Version 8 for Unix, Genetics Computer Group, University Research Park, 575 Science Drive, Madison, WI 53711). Bestfit uses the local homology algorithm of Smith and Waterman, *Advances in Applied Mathematics 2*: 482-489 (1981), to find the best segment of homology between two sequences. When using Bestfit or any other sequence alignment program to determine whether a particular sequence is, for instance, 95% identical to a reference sequence according to the present invention, the parameters are set, of course, such that the percentage of identity is calculated over the full length of the reference nucleotide sequence and that gaps in homology of up to 5% of the total number of nucleotides in the reference sequence are allowed.--

C23

At page 23, line 3, please replace the entire paragraph beginning "[t]he present application," with the following amended paragraph:

--The present application is directed to nucleic acid molecules comprising, or alternatively consisting of a nucleotide sequence at least 80%, 85%, 90%, 92%, 95%, 96%, 97%, 98%, or 99% identical to the nucleic acid sequence for example, shown in SEQ ID NO:1, irrespective of whether they encode a polypeptide having TR18 receptor activity. This is because even where a particular nucleic acid molecule does not encode a polypeptide having TR18 functional activity, one of skill in the art would still know how to use the nucleic acid molecule, for instance, as a hybridization probe or a polymerase chain reaction (PCR) primer. Uses of the nucleic acid molecules of the present invention that do not encode a polypeptide having TR18 receptor activity include, *inter alia:* (1) isolating the TR18 gene or allelic variants thereof in a cDNA library; (2) *in situ* hybridization (e.g., "FISH") to metaphase chromosomal spreads to provide precise chromosomal location of the TR18 receptor gene, as described in Verma *et al., Human Chromosomes: A Manual of Basic Techniques*, Pergamon Press, New York (1988); and (3) Northern Blot analysis for detecting TR18 receptor mRNA expression in specific tissues.--

C24

At page 23, line 17, please replace the entire paragraph beginning "[p]referred, however," with the following amended paragraph:

--Preferred, however, are nucleic acid molecules comprising, or alternatively consisting of, a nucleotide sequence at least 80%, 85%, 90%, 92%, 95%, 96%,

C25

97%, 98% or 99% identical to for example, the nucleic acid sequence shown in SEQ ID NO:1, which do, in fact, encode a polypeptide having TR18 functional activity. By "a polypeptide having TR18 functional activity" is intended polypeptides exhibiting activity similar, but not necessarily identical, to an activity of the TR18 receptor of the invention (either the full-length protein or, preferably, the mature protein), as measured in a particular biological assay.--

C25

At page 23, line 24, please replace the entire paragraph beginning "[o]f course, due to the degeneracy," and extending onto page 24, with the following amended paragraph:

--Of course, due to the degeneracy of the genetic code, one of ordinary skill in the art will immediately recognize that a large number of the nucleic acid molecules having a sequence at least 80%, 85%, 90%, 92%, 95%, 96%, 97%, 98%, or 99% identical to, for example, the nucleic acid shown in SEQ ID NO:1, will encode a polypeptide "having TR18-short functional activity." Similarly, a large number of the nucleic acid molecules having a sequence at least 80%, 85%, 90%, 92%, 95%, 96%, 97%, 98%, or 99% identical to, for example, a nucleic acid sequence shown in SEQ ID NO:1 will encode a polypeptide "having TR18 functional activity." In fact, since degenerate variants of these nucleotide sequences all encode the same polypeptide, this will be clear to the skilled artisan even without performing a biological assay. It will be further recognized in the art that, for such nucleic acid molecules that are not degenerate variants, a reasonable number will also encode a polypeptide having TR18 functional activity. This is because the skilled artisan is fully aware of amino acid substitutions that are either less likely or not likely to significantly effect protein function (e.g., replacing one aliphatic amino acid with a second aliphatic amino acid).--

C26

At page 43, line 25, please replace the entire paragraph beginning "[m]ultimers of the invention," and extending onto page 44, with the following amended paragraph:

--Multimers of the invention may be the result of hydrophobic, hydrophilic, ionic and/or covalent associations and/or may be indirectly linked, by for example, liposome formation. Thus, in one embodiment, multimers of the invention, such as, for example, homodimers or homotrimers, are formed when proteins of the invention contact one another in solution. In another embodiment, heteromultimers of the invention, such as, for example, heterotrimers or

C27

heterotetramers, are formed when proteins of the invention contact antibodies to the polypeptides of the invention (including antibodies to the heterologous polypeptide sequence in a fusion protein of the invention) in solution. In other embodiments, multimers of the invention are formed by covalent associations with and/or between the TR18 proteins of the invention. Such covalent associations may involve one or more amino acid residues contained in the polypeptide sequence of the protein (e.g., the polypeptide sequence shown in SEQ ID NO:2 or a polypeptide encoded by one of the deposited cDNA clones). In one instance, the covalent associations are cross-linking between cysteine residues located within the polypeptide sequences of the proteins which interact in the native (i.e., naturally occurring) polypeptide. In another instance, the covalent associations are the consequence of chemical or recombinant manipulation. Alternatively, such covalent associations may involve one or more amino acid residues contained in the heterologous polypeptide sequence in a TR18 fusion protein. In one example, covalent associations are between the heterologous sequence contained in a fusion protein of the invention (see, e.g., US Patent Number 5,478,925). In a specific example, the covalent associations are between the heterologous sequence contained in a TR18-Fc fusion protein of the invention (as described herein). In another specific example, covalent associations of fusion proteins of the invention are between heterologous polypeptide sequences from another TNF family ligand/receptor member that is capable of forming covalently associated multimers, such as for example, osteoprotegerin (see, e.g., International Publication No. WO 98/49305, the contents of which are herein incorporated by reference in its entirety). In another embodiment, two or more TR18 polypeptides of the invention are joined through synthetic linkers (e.g., peptide, carbohydrate or soluble polymer linkers). Examples include those peptide linkers described in U.S. Pat. No. 5,073,627 (hereby incorporated by reference). Proteins comprising multiple TR18 polypeptides separated by peptide linkers may be produced using conventional recombinant DNA technology.--

C27

At page 46, line 27, please replace the entire paragraph beginning "[a]ccordingly, in one embodiment," and extending onto page 47, with the following amended paragraph:

C28

--Accordingly, in one embodiment, the invention provides an isolated TR18 polypeptide having the amino acid sequence encoded by the amino acid sequence in SEQ ID NO:2, or a polypeptide comprising, or alternatively consisting of, a portion of the above polypeptides, such as for example, a mature TR18, the TR18 extracellular domain (amino acids 1 to 54 of SEQ ID NO:2), the TR18 cysteine rich motif (amino acids 8 to 41 of SEQ ID NO:2), and/or the TR18 intracellular domain (amino acids 81 to 184 of SEQ ID NO:2).--

At page 47, line 3, please replace the entire paragraph beginning "[p]olypeptide fragments of the present invention," with the following amended paragraph:

C29

--Polypeptide fragments of the present invention include polypeptides comprising or alternatively, consisting of: an amino acid sequence contained in SEQ ID NO:2; and encoded by a nucleic acid which hybridizes (e.g., under stringent hybridization conditions) to the complementary strand of the nucleotide sequence shown in SEQ ID NO:1, or a fragment thereof. Polynucleotides encoding these polypeptides are also encompassed by the invention.--

At page 47, line 9, the entire paragraph beginning "[p]rotein fragments may be," has been replaced by the following amended paragraph:

C30

--Protein fragments may be "free-standing," or comprised within a larger polypeptide of which the fragment forms a part or region, most preferably as a single continuous region. Representative examples of polypeptide fragments of the invention, include, for example, fragments that comprise or alternatively, consist of about amino acid residues: 1 to 7, 8 to 41, 41 to 54, 55 to 80, 81 to 104, 105 to 135, 136 to 165, and/or 166 to 184, of SEQ ID NO:2. In this context "about" includes the particularly recited ranges, ranges larger or smaller by several (5, 4, 3, 2, or 1) amino acids, at either extreme or at both extremes. Moreover, polypeptide fragments can be at least 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 110, 120, 130, 140, 150 or amino acids in length. Polynucleotides encoding these polypeptides are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.--

At page 47, line 20, please replace the entire paragraph beginning "[i]n additional embodiments," and extending onto page 48, with the following amended paragraph:

--In additional embodiments, the polypeptide fragments of the invention comprise, or alternatively consist of, one or more TR18 domains. Preferred polypeptide fragments of the present invention include one, two, three or more members selected from the group: (a) a polypeptide comprising or alternatively, consisting of, the TR18 extracellular domain (predicted to constitute amino acid residues 1 to 54 SEQ ID NO:2); (b) a polypeptide comprising or alternatively, consisting of, the TR18 cysteine rich domain (predicted to constitute amino acid residues 8 to 41 SEQ ID NO:2); (c) a polypeptide comprising or alternatively, consisting of, the TR18 transmembrane domain (predicted to constitute amino acid residues 55 to 80 SEQ ID NO:2); (d) a polypeptide comprising or alternatively, consisting of, the TR18 intracellular domain (predicted to constitute amino acid residues 81 to 184 SEQ ID NO:2); (e) a polypeptide comprising, or alternatively, consisting of, one, two, three, four or more, epitope bearing portions of the TR18 protein; or (f) any combination of polypeptides (a)-(e). Polynucleotides encoding these polypeptides are also encompassed by the invention.--

C31

At page 48, line 3, please replace the entire paragraph beginning "[a]s discussed above," with the following amended paragraph:

--As discussed above, it is believed that the extracellular cysteine rich motif of TR18 is important for interactions between TR18 and its ligands (e.g., Neutrokine-alpha and APRIL). Accordingly, in preferred embodiments, polypeptides of the invention comprise, or alternatively consist of amino acid residues 8 to 41 of SEQ ID NO:2. Proteins comprising or alternatively consisting of a polypeptide sequence which is at least 80%, 85%, 90%, 92%, 95%, 96%, 97%, 98% or 99% identical to the polypeptide sequences of the cysteine rich motif are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.--

C32

At page 48, line 11, please replace the entire paragraph beginning "[a]mong the especially preferred," with the following amended paragraph:

--Among the especially preferred fragments of the invention are fragments characterized by structural or functional attributes of TR18. Such fragments

C33

include amino acid residues that comprise alpha-helix and alpha-helix forming regions ("alpha-regions"), beta-sheet and beta-sheet-forming regions ("beta-regions"), turn and turn-forming regions ("turn-regions"), coil and coil-forming regions ("coil-regions"), hydrophilic regions, hydrophobic regions, alpha amphipathic regions, beta amphipathic regions, surface forming regions, and high antigenic index regions (i.e., containing four or more contiguous amino acids having an antigenic index of greater than or equal to 1.5, as identified using the default parameters of the Jameson-Wolf program) of complete (i.e., full-length) TR18 (SEQ ID NO:2). Certain preferred regions are those set out in Table 1 and include, but are not limited to, regions of the aforementioned types identified by analysis of the amino acid sequence depicted in SEQ ID NO:2, such preferred regions include; Garnier-Robson predicted alpha-regions, beta-regions, turn-regions, and coil-regions; Chou-Fasman predicted alpha-regions, beta-regions, and turn-regions; Kyte-Doolittle predicted hydrophilic; Hopp-Woods predicted hydrophobic regions; Eisenberg alpha and beta amphipathic regions; Emini surface-forming regions; and Jameson-Wolf high antigenic index regions, as predicted using the default parameters of these computer programs. Polynucleotides encoding these polypeptides are also encompassed by the invention.--

C33

At page 49, line 15, please replace the entire paragraph beginning "[a]ccordingly, the present invention," with the following amended paragraph:

--Accordingly, the present invention further provides polypeptides having one or more residues deleted from the amino terminus of the TR18 amino acid sequence shown in SEQ ID NO:2, up to the lysine residue at position number 179 and polynucleotides encoding such polypeptides. In particular, the present invention provides polypeptides comprising, or alternatively consisting of, the amino acid sequence of residues n^1-184 of SEQ ID NO:2, where n^1 is an integer from 2 to 179 corresponding to the position of the amino acid residue in SEQ ID NO:2.--

C34

At page 49, line 22, please replace the entire paragraph beginning "[m]ore in particular," and extending onto page 50, with the following amended paragraph:

--More in particular, the invention provides polynucleotides encoding polypeptides comprising, or alternatively consisting of, the amino acid sequence of residues: L-2

C35

to R-184; Q-3 to R-184; M-4 to R-184; A-5 to R-184; G-6 to R-184; Q-7 to R-184; C-8 to R-184; S-9 to R-184; Q-10 to R-184; N-11 to R-184; E-12 to R-184; Y-13 to R-184; F-14 to R-184; D-15 to R-184; S-16 to R-184; L-17 to R-184; L-18 to R-184; H-19 to R-184; A-20 to R-184; C-21 to R-184; I-22 to R-184; P-23 to R-184; C-24 to R-184; Q-25 to R-184; L-26 to R-184; R-27 to R-184; C-28 to R-184; S-29 to R-184; S-30 to R-184; N-31 to R-184; T-32 to R-184; P-33 to R-184; P-34 to R-184; L-35 to R-184; T-36 to R-184; C-37 to R-184; Q-38 to R-184; R-39 to R-184; Y-40 to R-184; C-41 to R-184; N-42 to R-184; A-43 to R-184; S-44 to R-184; V-45 to R-184; T-46 to R-184; N-47 to R-184; S-48 to R-184; V-49 to R-184; K-50 to R-184; G-51 to R-184; T-52 to R-184; N-53 to R-184; A-54 to R-184; I-55 to R-184; L-56 to R-184; W-57 to R-184; T-58 to R-184; C-59 to R-184; L-60 to R-184; G-61 to R-184; L-62 to R-184; S-63 to R-184; L-64 to R-184; I-65 to R-184; I-66 to R-184; S-67 to R-184; L-68 to R-184; A-69 to R-184; V-70 to R-184; F-71 to R-184; V-72 to R-184; L-73 to R-184; M-74 to R-184; F-75 to R-184; L-76 to R-184; L-77 to R-184; R-78 to R-184; K-79 to R-184; I-80 to R-184; S-81 to R-184; S-82 to R-184; E-83 to R-184; P-84 to R-184; L-85 to R-184; K-86 to R-184; D-87 to R-184; E-88 to R-184; F-89 to R-184; K-90 to R-184; N-91 to R-184; T-92 to R-184; G-93 to R-184; S-94 to R-184; G-95 to R-184; L-96 to R-184; L-97 to R-184; G-98 to R-184; M-99 to R-184; A-100 to R-184; N-101 to R-184; I-102 to R-184; D-103 to R-184; L-104 to R-184; E-105 to R-184; K-106 to R-184; S-107 to R-184; R-108 to R-184; T-109 to R-184; G-110 to R-184; D-111 to R-184; E-112 to R-184; I-113 to R-184; I-114 to R-184; L-115 to R-184; P-116 to R-184; R-117 to R-184; G-118 to R-184; L-119 to R-184; E-120 to R-184; Y-121 to R-184; T-122 to R-184; V-123 to R-184; E-124 to R-184; E-125 to R-184; C-126 to R-184; T-127 to R-184; C-128 to R-184; E-129 to R-184; D-130 to R-184; C-131 to R-184; I-132 to R-184; K-133 to R-184; S-134 to R-184; K-135 to R-184; P-136 to R-184; K-137 to R-184; V-138 to R-184; D-139 to R-184; S-140 to R-184; D-141 to R-184; H-142 to R-184; C-143 to R-184; F-144 to R-184; P-145 to R-184; L-146 to R-184; P-147 to R-184; A-148 to R-184; M-149 to R-184; E-150 to R-184; E-151 to R-184; G-152 to R-184; A-153 to R-184; T-154 to R-184; I-155 to R-184; L-156 to R-184; V-157 to R-184; T-158 to R-184; T-159 to R-184; K-160 to R-184; T-161 to R-184; N-162 to R-184; D-163 to R-184; Y-164 to R-184; C-165 to R-184; K-166 to R-184; S-167 to R-184; L-168 to R-184; P-169 to R-184; A-170 to

C3

R-184; A-171 to R-184; L-172 to R-184; S-173 to R-184; A-174 to R-184; T-175 to R-184; E-176 to R-184; I-177 to R-184; E-178 to R-184; and/or K-179 to R-184 of the TR18 sequence shown in SEQ ID NO:2. Polypeptides encoded by these polynucleotides are also encompassed by the invention.--

C35

At page 50, line 26, please replace the entire paragraph beginning "[i]n another embodiment," and extending onto page 51, with the following amended paragraph:

--In another embodiment, N-terminal deletions of the TR18 polypeptide can be described by the general formula n^2-54, where n^2 is a number from 2 to 50, corresponding to the position of amino acid identified in SEQ ID NO:2. Preferably, N-terminal deletions of the TR18 polypeptide of the invention shown as SEQ ID NO:2 include polynucleotides encoding polypeptides comprising, or alternatively consisting of, the amino acid sequence of residues L-2 to A-54; Q-3 to A-54; M-4 to A-54; A-5 to A-54; G-6 to A-54; Q-7 to A-54; C-8 to A-54; S-9 to A-54; Q-10 to A-54; N-11 to A-54; E-12 to A-54; Y-13 to A-54; F-14 to A-54; D-15 to A-54; S-16 to A-54; L-17 to A-54; L-18 to A-54; H-19 to A-54; A-20 to A-54; C-21 to A-54; I-22 to A-54; P-23 to A-54; C-24 to A-54; Q-25 to A-54; L-26 to A-54; R-27 to A-54; C-28 to A-54; S-29 to A-54; S-30 to A-54; N-31 to A-54; T-32 to A-54; P-33 to A-54; P-34 to A-54; L-35 to A-54; T-36 to A-54; C-37 to A-54; Q-38 to A-54; R-39 to A-54; Y-40 to A-54; C-41 to A-54; N-42 to A-54; A-43 to A-54; S-44 to A-54; V-45 to A-54; T-46 to A-54; N-47 to A-54; S-48 to A-54; and/or V-49 to A-54 of the TR18 extracellular domain sequence shown in SEQ ID NO:2. Polypeptides encoded by these polynucleotides are also encompassed by the invention.--

C36

At page 51, line 10, please replace the entire paragraph beginning "[i]n a most preferred embodiment," with the following amended paragraph:

--In a most preferred embodiment, the polypeptides of the invention comprise, or alternatively consist of amino acids M-4 to S-44 as shown in SEQ ID NO:2. Polypeptides at least 90%, at least 95%, at least 96%, at least 97%, and/or at least 99% identical to amino acids M-4 to S-44 as shown as SEQ ID NO:2 are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.--

C37

At page 51, line 16, please replace the entire paragraph beginning "[i]n another most preferred embodiment," with the following amended paragraph:

C38 --In another most preferred embodiment, the polypeptides of the invention comprise, or alternatively consist of amino acids M-4 to T-52 as shown in SEQ ID NO:2. Polypeptides at least 90%, at least 95%, at least 96%, at least 97%, and/or at least 99% identical to amino acids M-4 to T-52 as shown as SEQ ID NO:2 are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.--

At page 51, line 22, please replace the entire paragraph beginning "[i]n another most preferred embodiment," with the following amended paragraph:

C39 --In another most preferred embodiment, the polypeptides of the invention comprise, or alternatively consist of amino acids M-4 to A-54 as shown in SEQ ID NO:2. Polypeptides at least 90%, at least 95%, at least 96%, at least 97%, and/or at least 99% identical to amino acids M-4 to A-54 as shown as SEQ ID NO:2 are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.--

At page 52, line 10, please replace the entire paragraph beginning "[a]ccordingly, the present invention," with the following amended paragraph:

C40 --Accordingly, the present invention further provides polypeptides having one or more residues deleted from the carboxy terminus of the amino acid sequence of the TR18 polypeptide shown in SEQ ID NO:2, up to the glycine residue at position number 6, and polynucleotides encoding such polypeptides. In particular, the present invention provides polypeptides comprising the amino acid sequence of residues 1-m^1 of SEQ ID NO:2, where m^1 is an integer from 6 to 183 corresponding to the position of the amino acid residue in SEQ ID NO:2.--

At page 52, line 17, please replace the entire paragraph beginning "[m]ore in particular," and extending onto page 53, with the following amended paragraph:

C41 --More in particular, the invention provides polynucleotides encoding polypeptides comprising, or alternatively consisting of, the amino acid sequence of residues: M-1 to A-183; M-1 to S-182; M-1 to I-181; M-1 to S-180; M-1 to K-179; M-1 to E-178; M-1 to I-177; M-1 to E-176; M-1 to T-175; M-1 to A-174; M-1 to S-173; M-1

to L-172; M-1 to A-171; M-1 to A-170; M-1 to P-169; M-1 to L-168; M-1 to S-167; M-1 to K-166; M-1 to C-165; M-1 to Y-164; M-1 to D-163; M-1 to N-162; M-1 to T-161; M-1 to K-160; M-1 to T-159; M-1 to T-158; M-1 to V-157; M-1 to L-156; M-1 to I-155; M-1 to T-154; M-1 to A-153; M-1 to G-152; M-1 to E-151; M-1 to E-150; M-1 to M-149; M-1 to A-148; M-1 to P-147; M-1 to L-146; M-1 to P-145; M-1 to F-144; M-1 to C-143; M-1 to H-142; M-1 to D-141; M-1 to S-140; M-1 to D-139; M-1 to V-138; M-1 to K-137; M-1 to P-136; M-1 to K-135; M-1 to S-134; M-1 to K-133; M-1 to I-132; M-1 to C-131; M-1 to D-130; M-1 to E-129; M-1 to C-128; M-1 to T-127; M-1 to C-126; M-1 to E-125; M-1 to E-124; M-1 to V-123; M-1 to T-122; M-1 to Y-121; M-1 to E-120; M-1 to L-119; M-1 to G-118; M-1 to R-117; M-1 to P-116; M-1 to L-115; M-1 to I-114; M-1 to I-113; M-1 to E-112; M-1 to D-111; M-1 to G-110; M-1 to T-109; M-1 to R-108; M-1 to S-107; M-1 to K-106; M-1 to E-105; M-1 to L-104; M-1 to D-103; M-1 to I-102; M-1 to N-101; M-1 to A-100; M-1 to M-99; M-1 to G-98; M-1 to L-97; M-1 to L-96; M-1 to G-95; M-1 to S-94; M-1 to G-93; M-1 to T-92; M-1 to N-91; M-1 to K-90; M-1 to F-89; M-1 to E-88; M-1 to D-87; M-1 to K-86; M-1 to L-85; M-1 to P-84; M-1 to E-83; M-1 to S-82; M-1 to S-81; M-1 to I-80; M-1 to K-79; M-1 to R-78; M-1 to L-77; M-1 to L-76; M-1 to F-75; M-1 to M-74; M-1 to L-73; M-1 to V-72; M-1 to F-71; M-1 to V-70; M-1 to A-69; M-1 to L-68; M-1 to S-67; M-1 to I-66; M-1 to I-65; M-1 to L-64; M-1 to S-63; M-1 to L-62; M-1 to G-61; M-1 to L-60; M-1 to C-59; M-1 to T-58; M-1 to W-57; M-1 to L-56; M-1 to I-55; M-1 to A-54; M-1 to N-53; M-1 to T-52; M-1 to G-51; M-1 to K-50; M-1 to V-49; M-1 to S-48; M-1 to N-47; M-1 to T-46; M-1 to V-45; M-1 to S-44; M-1 to A-43; M-1 to N-42; M-1 to C-41; M-1 to Y-40; M-1 to R-39; M-1 to Q-38; M-1 to C-37; M-1 to T-36; M-1 to L-35; M-1 to P-34; M-1 to P-33; M-1 to T-32; M-1 to N-31; M-1 to S-30; M-1 to S-29; M-1 to C-28; M-1 to R-27; M-1 to L-26; M-1 to Q-25; M-1 to C-24; M-1 to P-23; M-1 to I-22; M-1 to C-21; M-1 to A-20; M-1 to H-19; M-1 to L-18; M-1 to L-17; M-1 to S-16; M-1 to D-15; M-1 to F-14; M-1 to Y-13; M-1 to E-12; M-1 to N-11; M-1 to Q-10; M-1 to S-9; M-1 to C-8; M-1 to Q-7; and/or M-1 to G-6 of the TR18 sequence shown in SEQ ID NO:2. Polypeptides encoded by these polynucleotides are also encompassed by the invention.--

C41

At page 53, line 17, please replace the entire paragraph beginning "[t]he invention also provides," with the following amended paragraph:

C42

--The invention also provides polynucleotides encoding polypeptides having one or more amino acids deleted from both the amino and the carboxyl termini, which may be described generally as having residues n^1-m^1 and/or n^2-m^1 of SEQ ID NO:2, where n^1, n^2, and m^1 are integers as described above. Thus, any of the above listed N- or C-terminal deletions can be combined to produce a polynucleotide encoding an N- and C-terminal deleted TR18 polypeptide.--

At page 53, line 23, please replace the entire paragraph beginning "[i]n a most preferred embodiment," with the following amended paragraph:

C43

--In a most preferred embodiment, the polypeptides of the invention comprise, or alternatively consist of amino acids M-4 to S-44, or M-4 to T-52, M-4 to A-54, as shown in SEQ ID NO:2. Polypeptides at least 90%, at least 95%, at least 96%, at least 97%, and/or at least 99% identical to amino acids M-4 to S-44, or M-4 to T-52, M-4 to A-54, as shown in SEQ ID NO:2 are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.--

At page 53, line 29, please replace the entire paragraph beginning "[t]he present invention encompasses," and extending onto page 54, with the following amended paragraph:

C44

--The present invention encompasses TR18 polypeptides comprising, or alternatively consisting of, an epitope of the polypeptide having an amino acid sequence of SEQ ID NO:2, or an epitope of a polypeptide sequence encoded by a polynucleotide that hybridizes to the complement of the sequence of SEQ ID NO:1 (e.g., under stringent hybridization conditions or lower stringency hybridization conditions as defined herein). The present invention further encompasses polynucleotide sequences encoding an epitope of a TR18 polypeptide sequence of the invention (such as, for example, the sequence disclosed in SEQ ID NO:2), polynucleotide sequences of the complementary strand of a polynucleotide sequence encoding an epitope of the invention, and polynucleotide sequences which hybridize to this complementary strand (e.g., under stringent hybridization conditions or lower stringency hybridization conditions defined herein).--

At page 55, line 13, please replace the entire paragraph beginning "[n]on-limiting examples," and extending onto page 56, with the following amended paragraph:

--Non-limiting examples of antigenic polypeptides of the invention include one, two, three, four, five, or more members selected from the group: a polypeptide comprising, or alternatively consisting of, amino acid residues from about Ser-9 to about Tyr-13 in SEQ ID NO:2; a polypeptide comprising, or alternatively consisting of, amino acid residues from about Cys-28 to about Asn-31 in SEQ ID NO:2; a polypeptide comprising, or alternatively consisting of, amino acid residues from about Val-49 to about Thr-52 in SEQ ID NO:2; a polypeptide comprising, or alternatively consisting of, amino acid residues from about Glu-105 to Asp-111 in SEQ ID NO:2; a polypeptide comprising, or alternatively consisting of, amino acid residues from about Lys-133 to about His-142 in SEQ ID NO:2; and a polypeptide comprising, or alternatively consisting of, amino acid residues from about Lys-160 to Lys-166 in SEQ ID NO:2. In this context, "about" means the particularly recited ranges and ranges that are larger or smaller by several, a few, 5, 4, 3, 2 or 1 amino acid residues at either or both the amino- and carboxy-termini. These polypeptide fragments have been determined to bear antigenic epitopes of the TR18 polypeptide by the analysis of the Jameson-Wolf antigenic index, as shown in Table I, above. Additional non-exclusive preferred antigenic epitopes include the antigenic epitopes disclosed herein, as well as portions thereof. Antigenic epitopes are useful, for example, to raise antibodies, including monoclonal antibodies that specifically bind the epitope. Preferred antigenic epitopes include the antigenic epitopes disclosed herein, as well as any combination of two, three, four, five or more of these antigenic epitopes. Antigenic epitopes can be used as the target molecules in immunoassays. (See, for instance, Wilson et al., Cell 37:767-778 (1984); Sutcliffe et al., Science 219:660-666 (1983)). Polynucleotides encoding these polypeptides are encompassed by the invention. Additionally, antibodies that bind to one or more of these polypeptides are also encompassed by the invention.--

C45

At page 58, line 12, please replace the entire paragraph beginning "[a]dditional fusion proteins," with the following amended paragraph:

--Additional fusion proteins of the invention may be generated through the techniques of gene shuffling, motif shuffling, exon shuffling, and/or codon-shuffling (collectively referred to as "DNA shuffling"). DNA shuffling may be employed to modulate the activities of polypeptides of the invention, such methods can be used to generate polypeptides with altered activity, as well as agonists and antagonists of the polypeptides. See, generally, U.S. Patent Nos. 5,605,793; 5,811,238; 5,830,721; 5,834,252; and 5,837,458, and Patten et al., Curr. Opinion Biotechnol. 8:724-33 (1997); Harayama, Trends Biotechnol. 16(2):76-82 (1998); Hansson, et al., J. Mol. Biol. 287:265-76 (1999); and Lorenzo and Blasco, Biotechniques 24(2):308-13 (1998) (each of these patents and publications are hereby incorporated by reference in its entirety). In one embodiment, alteration of TR18 polynucleotides corresponding to SEQ ID NO:1 and the polypeptides encoded by these polynucleotides may be achieved by DNA shuffling. DNA shuffling involves the assembly of two or more DNA segments by homologous or site-specific recombination to generate variation in the polynucleotide sequence. In another embodiment, polynucleotides of the invention, or the encoded polypeptides, may be altered by being subjected to random mutagenesis by error-prone PCR, random nucleotide insertion or other methods prior to recombination. In another embodiment, one or more components, motifs, sections, parts, domains, fragments, etc., of a polynucleotide encoding a polypeptide of the invention may be recombined with one or more components, motifs, sections, parts, domains, fragments, etc. of one or more heterologous molecules.--

C46

At page 59, line 10, please replace the entire paragraph beginning "[t]hus, the fragment," with the following amended paragraph:

--Thus, the fragment, derivative, or analog of the polypeptide of SEQ ID NO:2, may be (i) one in which at least one or more of the amino acid residues are substituted with a conserved or non-conserved amino acid residue (preferably a conserved amino acid residue(s), and more preferably at least one but less than ten conserved amino acid residues) and such substituted amino acid residue may or may not be one encoded by the genetic code, or (ii) one in which one or more of

C46

the amino acid residues includes a substituent group, or (iii) one in which the mature polypeptide is fused with another compound, such as a compound to increase the half-life of the polypeptide (for example, polyethylene glycol), or (iv) one in which the additional amino acids are fused to the mature polypeptide, such as an IgG Fc fusion region peptide or leader or secretory sequence or a sequence which is employed for purification of the mature polypeptide or a proprotein sequence. Such fragments, derivatives and analogs are deemed to be within the scope of those skilled in the art from the teachings herein.--

C47

At page 60, line 14, please replace the entire paragraph beginning "[i]n specific embodiments," with the following amended paragraph:

--In specific embodiments, the number of substitutions, additions or deletions in the amino acid sequence of SEQ ID NO:2 and/or any of the polypeptide fragments described herein (e.g., the cysteine rich motif, the extracellular domain and/or intracellular domain) is 75, 70, 60, 50, 40, 35, 30, 25, 20, 15, 10, 9, 8, 7, 6, 5, 4, 3, 2, 1 or 30-20, 20-15, 20-10, 15-10, 10-1, 5-10, 1-5, 1-3 or 1-2.--

C48

At page 69, line 10, please replace the entire paragraph beginning "[t]he polypeptide of the present invention," with the following amended paragraph:

--The polypeptides of the present invention include a polypeptide comprising, or alternatively, consisting of: amino acids 1 to 184 in SEQ ID NO:2; amino acids 2 to 184 in SEQ ID NO:2; the TR18 extracellular domain; the TR18 cysteine rich motif; the TR18 transmembrane domain; the intracellular domain of TR18; and the TR18 extracellular domain and the TR18 intracellular domain with all or part of the transmembrane domain deleted; as well as polypeptides which are at least 80% identical, more preferably at least 90% or 95% identical, still more preferably at least 96%, 97%, 98%, 99% or 100% identical to the polypeptides described above (e.g., the polypeptide of SEQ ID NO:2), and also include portions of such polypeptides with at least 30 amino acids and more preferably at least 50 or at least 100 amino acids. Polynucleotides encoding these polypeptides are also encompassed by the invention.--

C49

At page 70, line 3, please replace the entire paragraph beginning "[a]s a practical matter," with the following amended paragraph:

--As a practical matter, whether any particular polypeptide is at least 85%, 90%, 92%, 95%, 96%, 97%, 98%, or 99% identical to, for instance, the amino acid sequence shown in SEQ ID NO:2, can be determined conventionally using known computer programs such the Bestfit program (Wisconsin Sequence Analysis Package, Version 8 for Unix, Genetics Computer Group, University Research Park, 575 Science Drive, Madison, WI 53711). When using Bestfit or any other sequence alignment program to determine whether a particular sequence is, for instance, 95% identical to a reference sequence according to the present invention, the parameters are set, of course, such that the percentage of identity is calculated over the full length of the reference amino acid sequence and that gaps in homology of up to 5% of the total number of amino acid residues in the reference sequence are allowed.--

C50

At page 71, line 21, please replace the entire paragraph beginning "[i]n additional embodiments," with the following amended paragraph:

--In additional embodiments, polynucleotides of the invention comprise, or alternatively consist of, a polynucleotide sequence at least 80%, 85%, 90%, 92%, 95%, 96%, 97%, 98%, 99% or 100% identical to the polynucleotide sequence encoding the extracellular cysteine rich motif of TR18 disclosed in SEQ ID NO:2 (amino acid residues from 8 to 41). In another embodiment, the invention provides an isolated nucleic acid molecule comprising a polynucleotide that hybridizes under stringent hybridization conditions to DNA complementary to the polynucleotide sequence encoding the TR18 extracellular cysteine rich motif. The present invention also encompasses the above polynucleotide/nucleic acid sequences fused to a heterologous polynucleotide sequence. Polypeptides encoded by these nucleic acids and/or polynucleotide sequences are also encompassed by the invention.--

C51

At page 75, line 14, please replace the entire paragraph beginning "[a]ntibodies of the present invention," with the following amended paragraph:

--Antibodies of the present invention may be described or specified in terms of the epitope(s) or portion(s) of a polypeptide of the present invention which they

C52

recognize or specifically bind. The epitope(s) or polypeptide portion(s) may be specified as described herein, e.g., by N-terminal and C-terminal positions, by size in contiguous amino acid residues, or listed in the Tables. Antibodies which specifically bind any epitope or polypeptide of the present invention may also be excluded. Therefore, the present invention includes antibodies that specifically bind polypeptides of the present invention, and allows for the exclusion of the same.--

C52

At page 220, line 22, please replace the entire paragraph beginning "[o]ligonucleotides that are complementary," and extending onto page 221, with the following amended paragraph:

--Oligonucleotides that are complementary to the 5' end of the message, *e.g.*, the 5' untranslated sequence up to and including the AUG initiation codon, should work most efficiently at inhibiting translation. However, sequences complementary to the 3' untranslated sequences of mRNAs have been shown to be effective at inhibiting translation of mRNAs as well. See generally, Wagner, R., 1994, Nature 372:333-335. Thus, oligonucleotides complementary to either the 5'- or 3'- non-translated, non-coding regions of TR18 shown in SEQ ID NO:1, respectively, could be used in an antisense approach to inhibit translation of endogenous TR18 mRNA. Oligonucleotides complementary to the 5' untranslated region of the mRNA should include the complement of the AUG start codon. Antisense oligonucleotides complementary to mRNA coding regions are less efficient inhibitors of translation but could be used in accordance with the invention. Whether designed to hybridize to the 5'-, 3'- or coding region of TR18 mRNA, antisense nucleic acids should be at least six nucleotides in length, and are preferably oligonucleotides ranging from 6 to about 50 nucleotides in length. In specific aspects the oligonucleotide is at least 10 nucleotides, at least 17 nucleotides, at least 25 nucleotides or at least 50 nucleotides.--

C53

At page 222, line 23, pleaser replace the entire paragraph beginning "[p]otential antagonists," and extending onto page 223, with the following amended paragraph:

--Potential antagonists according to the invention also include catalytic RNA, or a ribozyme (See, e.g., PCT International Publication WO 90/11364, published October 4, 1990; Sarver et al, Science 247:1222-1225 (1990). While ribozymes

C54

that cleave mRNA at site specific recognition sequence can be used to destroy TR18 mRNAs, the use of hammerhead ribozymes is preferred. Hammerhead ribozymes cleave mRNAs at locations dictated by flanking regions that form complementary base pairs with the target mRNA. The sole requirement is that the target mRNA have the following sequence of two bases: 5'-UG-3'. The construction and production of hammerhead ribozymes is well known in the art and is described more fully in Haseloff and Gerlach, Nature 334:585-591 (1988). There are numerous potential hammerhead ribozyme cleavage sites within the nucleotide sequence TR18 (SEQ ID NO:1). Preferably, the ribozyme is engineered so that the cleavage recognition site is located near the 5' end of the TR18 mRNA; i.e., to increase efficiency and minimize the intracellular accumulation of non-functional mRNA transcripts.--

C54

At page 224, line 3, please replace the entire paragraph beginning "[i]n other embodiments," with the following amended paragraph:

--In other embodiments, antagonists according to the present invention include soluble forms of TR18 (e.g., fragments of TR18 shown in SEQ ID NO:2 that include one or more copies of the cysteine rich motif from the extracellular domain of TR18). Such soluble forms of the TR18, which may be naturally occurring or synthetic, antagonize TR18 mediated signaling by competing with native TR18 for binding to Neutrokine-alpha (See, U.S. Application Serial No. 60/188,208), and/or by forming a multimer that may or may not be capable of binding the receptor, but which is incapable of inducing signal transduction. Preferably, these antagonists inhibit TR18 mediated stimulation of lymphocyte (e.g., B-cell) proliferation, differentiation, and/or activation. Antagonists of the present invention also include antibodies specific for TNFR-family receptors and TR18-Fc fusion proteins.--

C55

At page 224, line 26, please replace the entire paragraph beginning "[a]ntagonists of the present invention," and extending onto page 225, with the following amended paragraph:

--Antagonists of the present invention also include antibodies specific for TNF-family ligands or the TR18 polypeptides of the invention. Antibodies according to the present invention may be prepared by any of a variety of standard methods using TR18 immunogens of the present invention. As indicated, such TR18

C56